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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,254	06/01/2005	Richard E. Walters	05-084	1412
<div>7590 Marvin S Townsend Patent Attorney 8 Grovepoint Court Rockville, MD 20854</div>				
<div>EXAMINER FERNANDEZ, SUSAN EMILY</div>				
<div>ART UNIT 1651</div>				
<div>PAPER NUMBER</div>				
<div>MAIL DATE 08/19/2009</div>				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/537,254

Applicant(s)

WALTERS ET AL.

Examiner

SUSAN E. FERNANDEZ

Art Unit

1651

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8, 16, 19-22, 24, 25, 28, 29, 31, 35, 38, 39, 42 and 45 is/are pending in the application.
- 4a) Of the above claim(s) 24 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8, 16, 19-22, 28, 29, 31, 35, 38, 39, 42 and 45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Final Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The amendment filed May 6, 2009, has been received and entered.

Claims 1-6, 8, 16, 19-22, 24, 25, 28, 29, 31, 35, 38, 39, 42, and 45 are pending.

Claims 24 and 25 are withdrawn.

Claims 1-6, 8, 16, 19-22, 28, 29, 31, 35, 38, 39, 42, and 45 are examined on the merits to the extent they read on the elected subject matter.

Specification

The amendment filed May 6, 2009, is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

First, the paragraph on page 21, spanning lines 5-7, has been amended from "a range spanning 2 to 10 milliliters" to "above 2 milliliters" which have different scopes. A range of "above 2 milliliters" encompasses volumes greater than 10 milliliters, which is not supported in the specification.

The paragraph on page 23, spanning line 9-13, has been amended to indicate that the conductivity in Figure 2 is in a range spanning 0.001 to 100 milliSiemens/cm. However, the lower limit in Figure 2 is clearly 0.01 milliSiemens/cm. The paragraph also states that the Geometric Factor ranges to as much as "less than or equal to 0.100000 cm-1." However, Figure 2 shows that the upper limit is 10.000000 cm-1. Finally, the paragraph also has been amended to

indicate that the resistance is greater than one ohm. However, this does not appear to be evident in Figure 2.

The paragraph on page 27, spanning lines 14-22, has been amended to recite that the chamber volume is 2 milliliters rather than 1 milliliter. However, it is unclear that there is support for the amendment.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 16, 19-22, 28, 29, 31, 35, 38, 39, 42, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meserol (US 5,720,921).

Meserol discloses a method and apparatus for the encapsulation of biologically-active substances in red blood cells, which can be performed in an automated, continuous-flow, self contained electroporation system (abstract). The method and apparatus can be used broadly for the incorporation of a variety of biologically-active substances in cells and lipid vesicles (column 8, lines 10-12). The apparatus is self-contained and therefore sterile (column 9, lines 22-23), thus limitations in instant claims 2 and 4 are met. Moreover, it is clear from Figure 1 that the apparatus has entry and exit ports and multiple reservoirs (thus meeting limitations in instant claims 5, 38, and 39). Note that high voltage square pulses (2.13 kV/cm, 2 ms) can be administered followed by a lower voltage exponential pulse (1.5 to 1.75 kV/cm, 5 ms) for the increased encapsulation of IHP into red blood cells (column 13, lines 23-27). Thus, limitations in instant claims 8 and 16 are met.

The method of Meserol is performed statically since Meserol teaches that "A conventional electroporation chamber may be used when the operation of the apparatus is static..." (column 15, lines 5-7). In the method, single discrete batches can be processed (column 15, lines 5-7) and the distance between the electrodes will vary depending on the flow volume and field strength (column 15, lines 11-12). Though it is in reference to a continuous flow cell, it would have been obvious that distance between electrodes would have been varied when performing the method statically in order to obtain different effects. The distance between electrodes would have been result-effective. Note that parallel plate electrodes can be used, as demonstrated in Figures 9 and 10 (see column 22, lines 24-26), thus meeting limitations in instant claim 6. Moreover, limitations in instant claim 35 are taught by the reference given that gases are removed by cylinders (column 26, lines 27-29). Finally, the resulting cells can be used

for therapeutic purposes (column 28, lines 8-27), thus meeting limitations in instant claims 20 and 21.

Meserol differs from the claimed invention in that it does not expressly disclose that the geometric factor of the chamber which includes the electrodes is less than or equal to 0.1 cm^{-1} or that the suspension in the apparatus has a conductivity in a range spanning 0.001 to 100 milliSiemens/cm.

Hibi et al. discloses that a method of transfecting cells with nucleic acids wherein a flow chamber is used having a volume of 50 μL and an inter-electrode distance of 0.5 mm (column 6, lines 19-23). This results in a geometric factor less than or equal to 0.1 cm^{-1} .

At the time the invention was made, it would have been obvious to have used the geometric factor of Hibi et al. as the geometric factor of the Meserol apparatus. One of ordinary skill in the art would have been motivated to do this since there would have been a reasonable expectation of success in obtaining electroporation with such a geometric factor. Moreover, varying the volume, the electrode distance, and solution conductivity would have been a matter of routine experimentation, particularly since Meserol indicates that the distance between electrodes will vary depending on the flow volume and field strength (column 15, lines 11-12). Thus, claims 1-6, 8, 16, 19, 20, 21, 28, 29, 31, 35, 38, 39, 42, and 45 are rendered obvious.

Claim 22 is also rendered obvious since Hibi et al. demonstrates that a flow electroporation device is suitable for inserting nucleic acids into cells.

A holding of obviousness is clearly required.

Response to Arguments

Applicant's arguments filed May 6, 2009, have been fully considered but they are not persuasive. The applicant asserts that Meserol does not disclose sequential batch electroporation. However, Meserol teaches that single discrete batches can be processed (column 15, lines 5-7) and that a flow electroporation chamber may be used (column 15, lines 7-9). Though the prior art (Meserol or Hibi et al) do not define the "geometric factor," the geometric factor indeed exists given that there is an electrode gap and a chamber volume. Moreover, the applicant indirectly asserts a geometric factor for Meserol in Exhibit A.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The features are discussed in further detail below.

On page 17 of the arguments, the applicant asserts that the heating is reduced in the claimed invention. The arguments on page 24 also speak of the creation of quite a bit of unwanted heat when practicing the Meserol invention. However, this feature is not recited in the instant claims. Moreover, on page 18 of the arguments, the applicants assert that the electric fields can be complex and not constrained by the flow rates in flow systems, but these features are not recited in the instant claims.

In response to applicant's argument based upon the age of the references (at several instances in the response filed), contentions that the reference patents are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its

presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

With respect to the assertion that Meserol teaches away from static electroporation, it is respectfully pointed out that "A conventional electroporation chamber may be used when the operation of the apparatus is static..." (column 15, lines 5-7). Moreover, the over heating that is discussed in Meserol is only in reference to continuous use.

While Meserol does not teach the recited geometric factor, it is respectfully noted that Hibi et al. teaches this aspect of the claimed invention. Moreover, varying the volume, the electrode distance, and solution conductivity would have been a matter of routine experimentation.

The applicant also asserts that while Meserol teaches very short lengths of time for electric field application, the claimed invention provides for electric field lengthy durations. However, this feature is not recited in the instant claims.

Hibi et al. is applied only for its teachings of the recited geometric factor and the teaching of insertion of nucleic acids into cells, not for teachings with respect to conductivity, electrical resistance, or performing the methods statically.

The applicant also argues that neither Hibi et al. or Meserol teach a formula or graphical method of scaling up. It is respectfully noted that the instant claims do not speak of scaling up. Further still, the applicant asserts that Hibi et al. differs from the claimed invention in that the claimed invention can successfully be conducted at room temperature. However, the instant claims do not speak of temperature.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **SUSAN E. FERNANDEZ** whose telephone number is (571)272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Susan E. Fernandez
Examiner
Art Unit 1651

sef